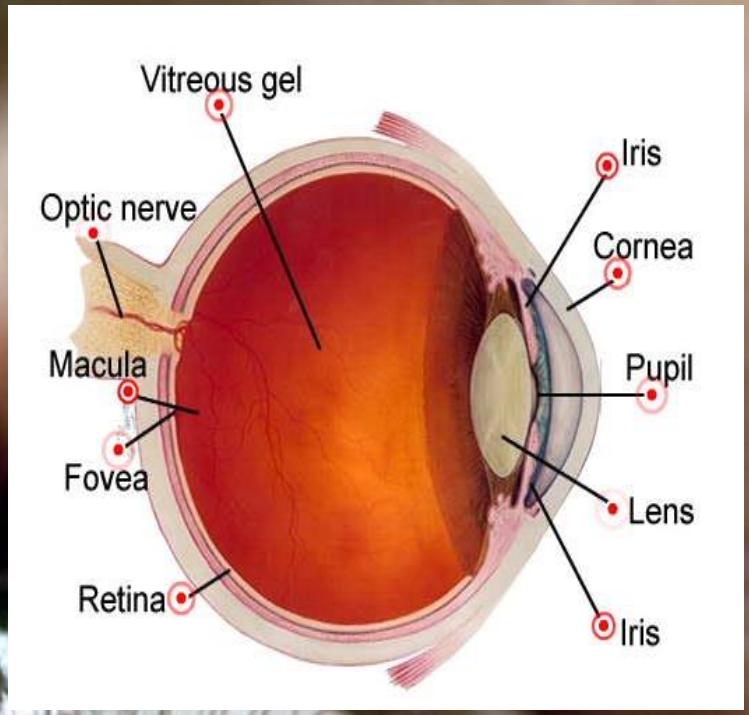
OCULAR PHARMACOLOGY

CHALLENGES TO DRUG DELIVERY TO THE EYE

Blood- retinal, blood- aqueous, blood- vitreous barriers prevent high concentration of drugs passage from the blood stream

Most agents injected into the vitreous are cleared rapidly and therefore are ineffective

Subconjunctival and intravitreal injections carry a risk of infection



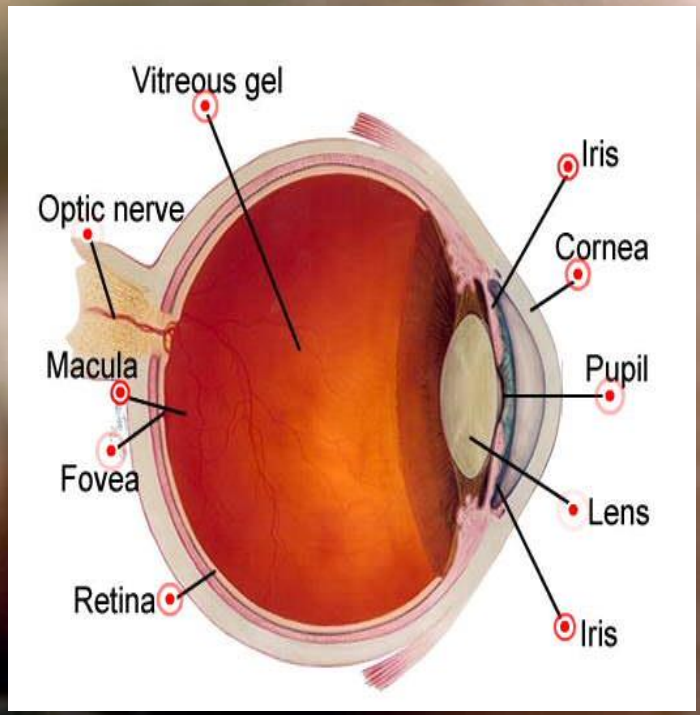
OCULAR PHARMACOLOGY

ILOS

Outline common routes of administration of drugs to the eye

Discuss the pharmacokinetics of drugs applied topically to the eye

Classify drugs used for treatment of disorders of the eye



Elaborate on autonomic, anti-inflammatory drugs & drugs used for glaucoma

Hint on ocular toxicity of some drugs

ROUTES OF ADMINISTRATION

1- Topical

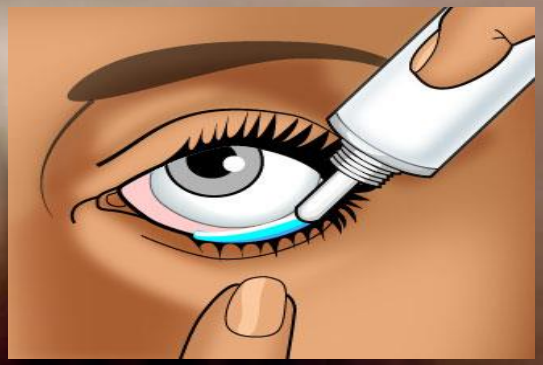
Eye drops

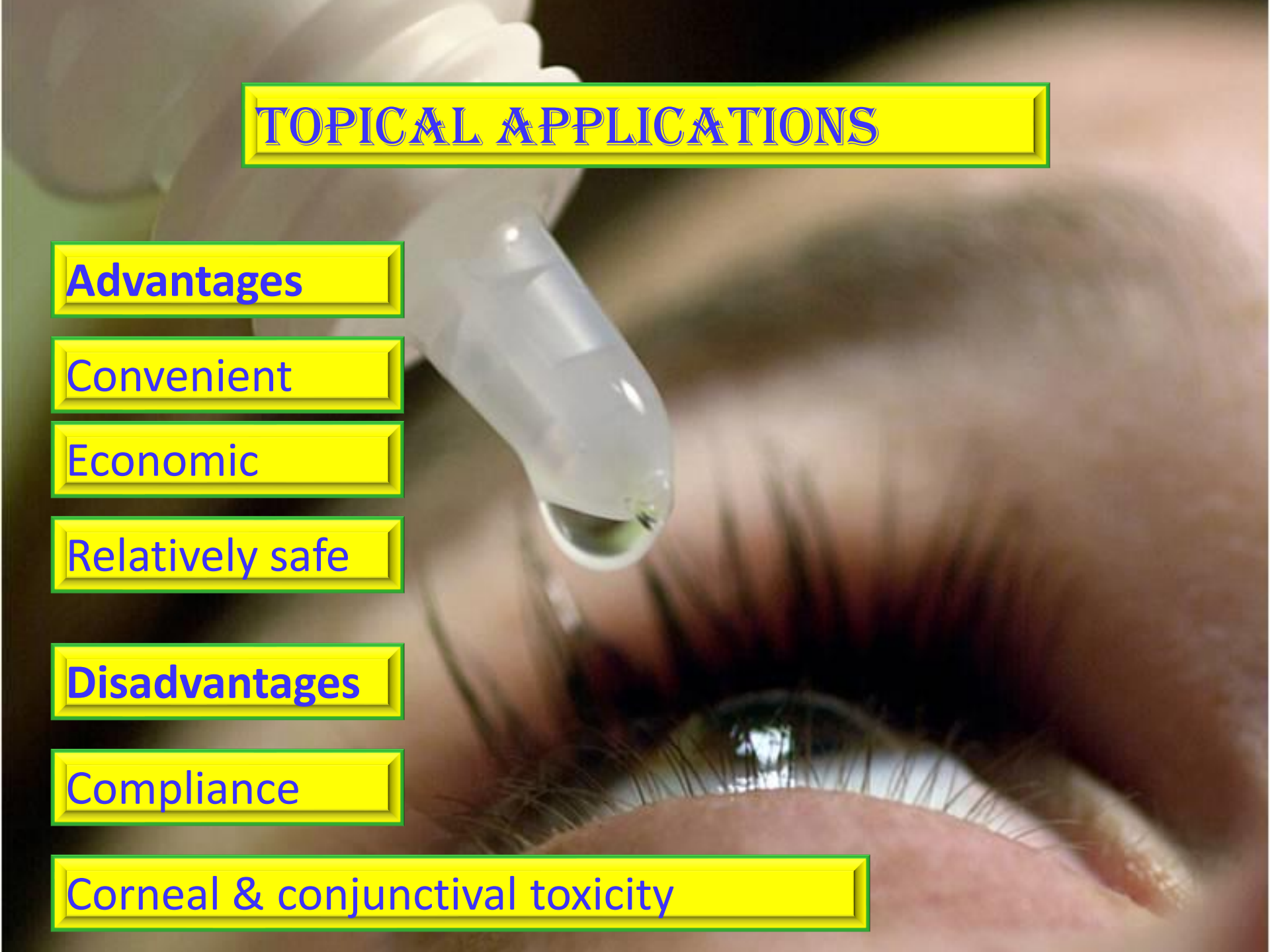
Ointments

Injections

2- Systemic

Oral, IV





TOPICAL APPLICATIONS

Advantages

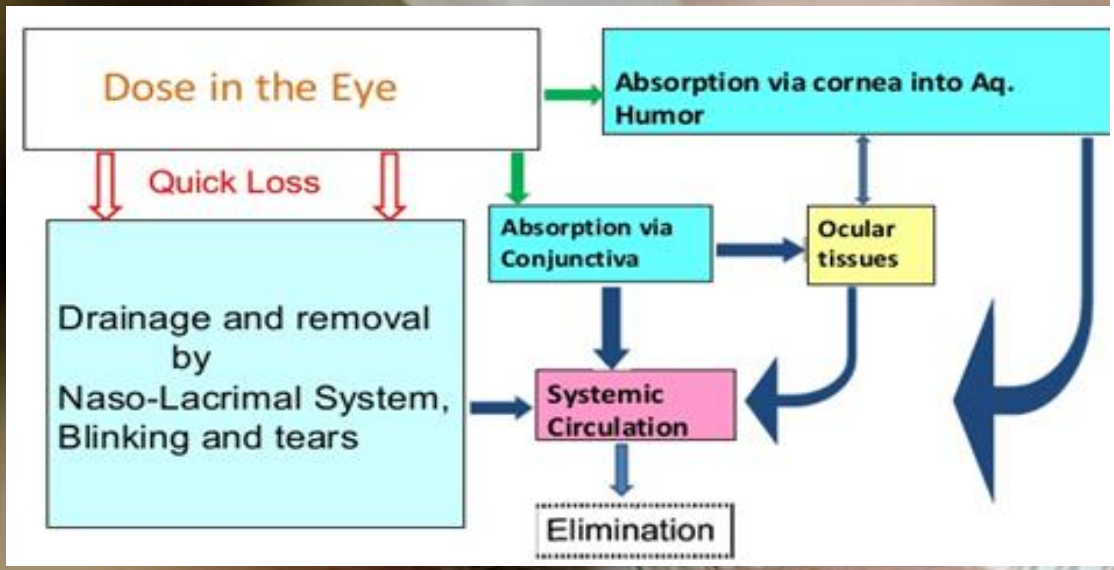
- Convenient
- Economic
- Relatively safe

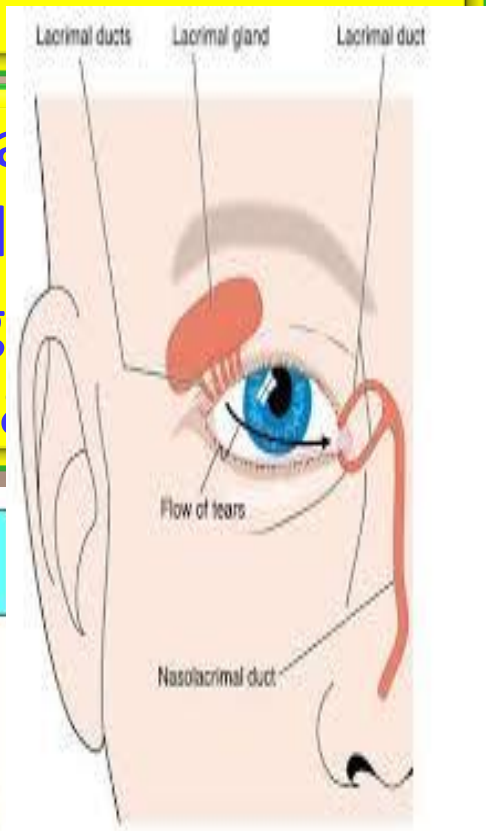
Disadvantages

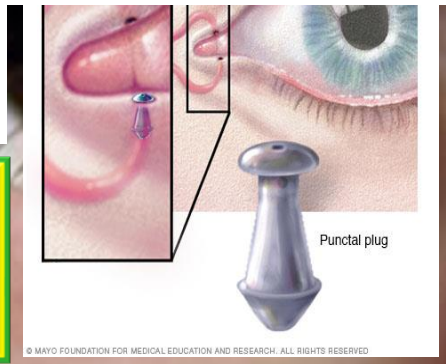
- Compliance
- Corneal & conjunctival toxicity

PHARMACOKINETICS OF TOPICAL APPLICATIONS

Absorption: After topical application, rate of a
determined by the time drug remains in cul-d
elimination by nasolacrimal drainage, binding
protein, metabolism, diffusion across cornea







Drug residence time can be prolonged by plugging tear ducts or change of formulation

PHARMACOKINETICS

Distribution: After corneal absorption, the drug accumulates in the aqueous humor , intraocular structures or systemically distributed.

Melanin binding prolongs the effect of α -agonists in patients with dark pigmented iris.

Chloroquine binds to retinal pigment →↓ visual acuity.

Metabolism: Significant biotransformation takes place in the eye.

Esterases activate pro drugs e.g. dipivefrin → (adrenaline), latanoprost →($PGF_{2\alpha}$)

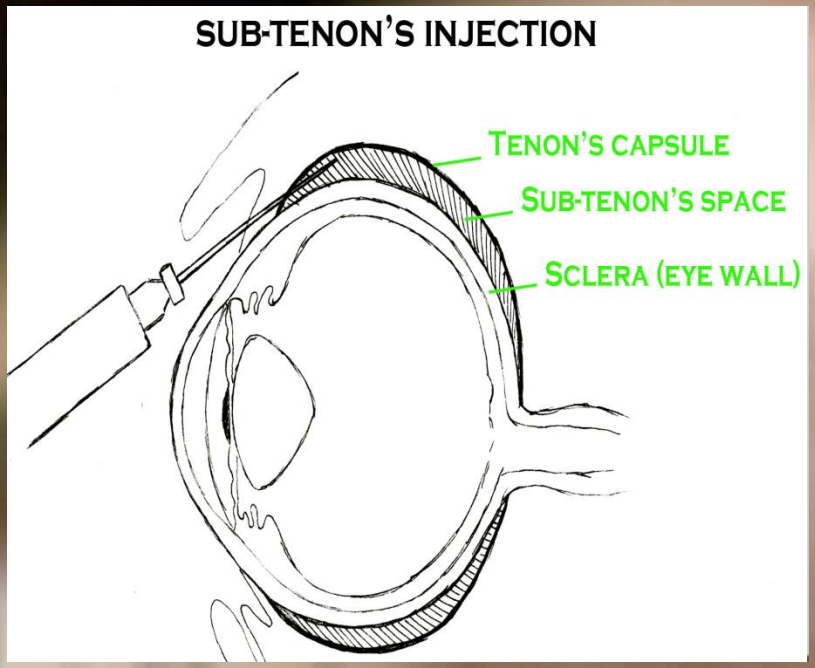
LOCAL INJECTIONS

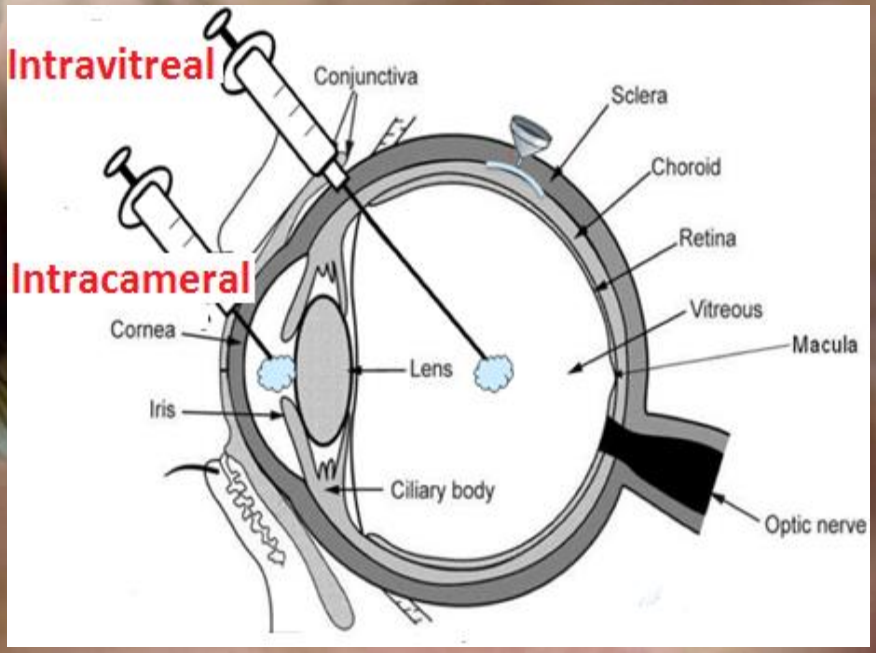
i- Periocular

Subconjunctival, peribulbar, retrobulbar, or subtenon

ii- Intraocular

Intracameral or intravitreal





PERI-OCULAR INJECTIONS

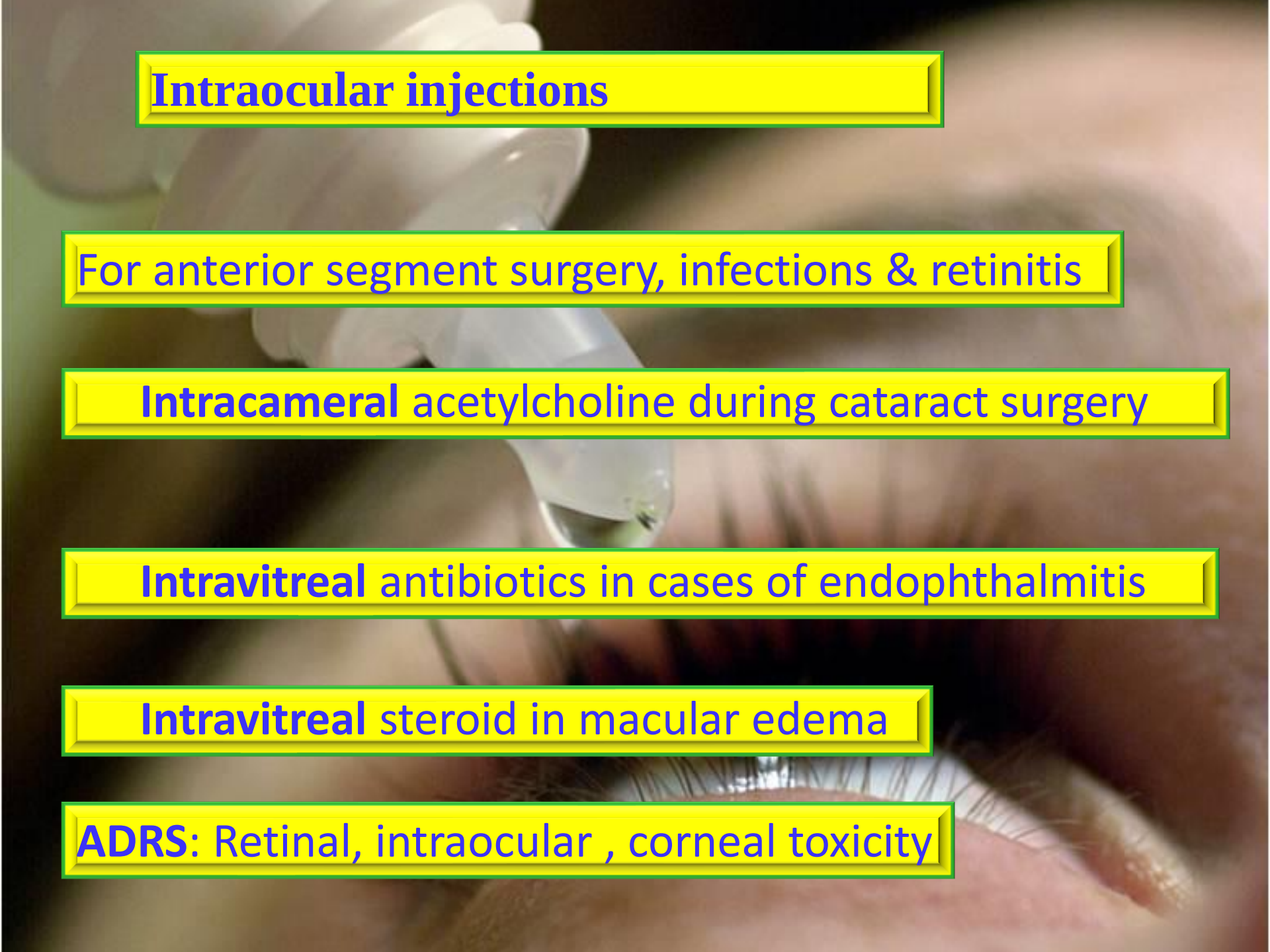
- Subconjunctival, subtenon, peribulbar, or retrobulbar

For infection of anterior segment and inflammation of uvea

- bypass the conjunctival and corneal epithelium which is good for drugs with low lipid solubility (e.g. penicillins)

- **steroid and local anesthetics**

Local toxicity, tissue injury, globe perforation, optic nerve damage


Intraocular injections
For anterior segment surgery, infections & retinitis
Intracameral acetylcholine during cataract surgery
Intravitreal antibiotics in cases of endophthalmitis
Intravitreal steroid in macular edema
ADRS: Retinal, intraocular , corneal toxicity

SYSTEMIC DRUGS

Factor influencing systemic drug penetration into ocular tissue

lipid solubility of the drug: more penetration with high lipid solubility

Protein binding: more effect with low protein binding

Eye inflammation: more penetration with ocular inflammation

OCULAR DRUGS

Autonomic drugs

Miotics
Mydriatics
Cycloplegics

Antiglaucoma Drugs

Anti-inflammatory drugs

Steroids & NSAIDs

Chemotherapeutics

Antibacterial, antifungal, antiviral, antimitotic

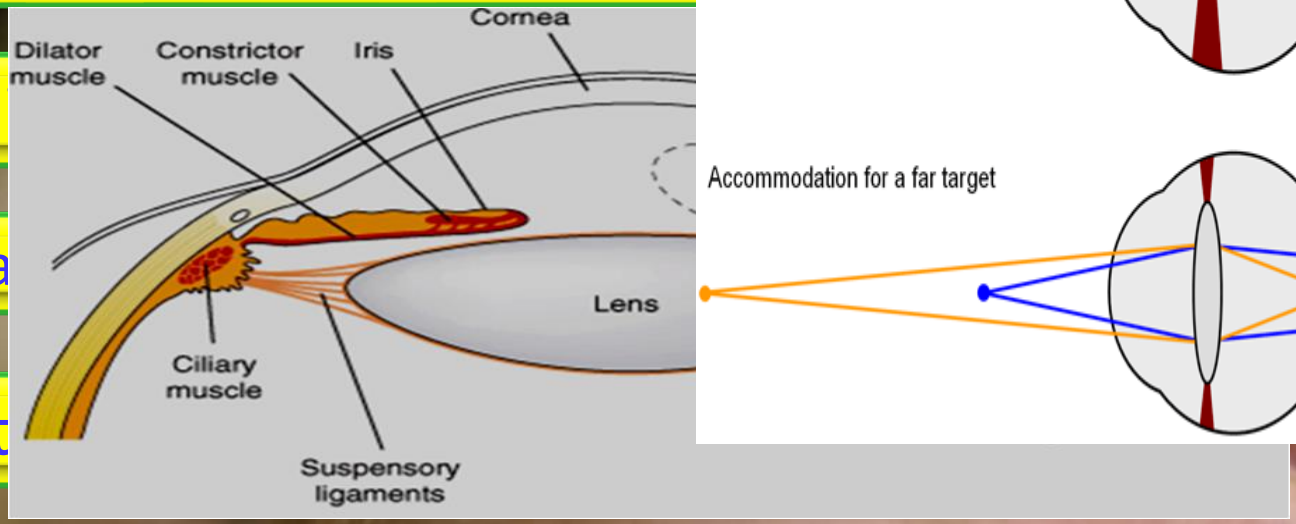
Local anesthetics

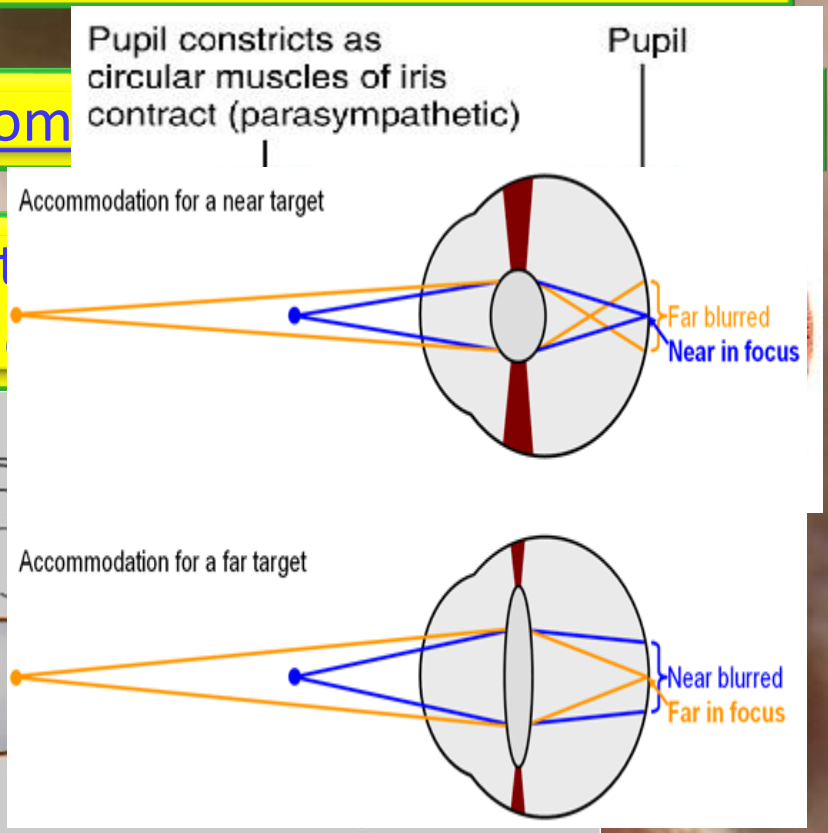
Ocular lubricants

AUTONOMIC DRUGS

Parasympathetic Drugs

- Constriction of the pupillary sphincter muscle **(miosis)**
- Contraction of the ciliary muscle (accom
- Increase aqueous outflow through t canal of Schlemm by ciliary muscle
- Decrease
- Increase la
- Conjunct





PARASYMPATHETIC DRUGS

Clinical uses

Glauco

Counte

-To bre

-In acc

-In lice

Ocular

Diminished vision (myopia), headache

Drugs	Ocular uses
Acetycholine Carbachol Methacholine	Induction of miosis in surgery Glaucoma
Pilocarpine	In open angle glaucoma
Physostigmine	Glaucoma, accommodative esotropia
Ecothiophate	Glaucoma, accommodative esotropia

CHOLINERGIC ANTAGONISTS

- **Mydriasis** *due to relaxation of circular muscles*
- **Cycloplegia** (loss of near accommodation) due to relaxation of ciliary muscles

Loss of light reflex

Increased I.O.P

- ↓ Lacrimal secretion → sandy eye

CHOLINERGIC ANTAGONISTS

Clinical uses

-To prevent adhesion in uveitis & iritis

-Funduscopic examination of the eye

-Measurement of refractive error

ADRENERGIC AGONISTS

Non-selective agonists

Mechanism: ↑ uveoscleral outflow of aqueous humor

Uses: open angle glaucoma

α_1 agonists e.g. phenylepherine

Mydriasis (without cycloplegia)

-Funduscopic examination of the eye

-Decongestant in minor allergic hyperemia of eye

-To prevent adhesion in uveitis & iritis

ADRENERGIC AGONISTS

α_2 agonists e.g. apraclonidine

Mechanism: ↓ production of aqueous humor

Uses: glaucoma treatment, Prophylaxis against IOP spiking after glaucoma laser procedures

β- BLOCKERS

non-selective: timolol, carteolol

selective: betaxolol (beta 1 "cardioselective")

Mechanism: Act on ciliary body to ↓ production of aqueous humor

Uses: open angle glaucoma

Advantages can be used in patients with hypertension/ischemic heart disease

Ocular ADRS:- irritation

TREATMENT OF OPEN ANGLE GLAUCOMA (CHRONIC)

Goal is to decrease IOP

- Decreasing production of aqueous humor

B- blockers
α_2 agonists
Carbonic anhydrase inhibitors

- Increasing outflow of aqueous humor

Prostaglandins
Adrenergic agonists (non-specific)
Parasympathomimetics

CARBONIC ANHYDRASE INHIBITORS

Acetazolamide (oral), Dorzolamide (topical)

Mechanism:-↓ production of aqueous humor

Side Effects:
myopia, malaise, anorexia, GI upset, headache
metabolic acidosis, renal stone,

Contraindications:
sulpha allergy, digitalis users, pregnancy

PROSTAGLANDINS

Latanoprost

Mechanism: ↑Uveoscleral outflow

Uses: open angle glaucoma

Administration: Topical drops

Side Effects: Iris color change

DRUG THERAPY OF ACUTE ANGLE CLOSURE GLAUCOMA (NARROW ANGLE)

Acute, painful increases of pressure

Is associated with occlusion of the outflow drainage pathway

Emergency situation that require treatment before surgery (Iridectomy)

Oral Acetazolamide

Topical cholinomimetics e.g.: pilocarpine

Dehydrating agents: IV infusion Of hypertonic solution (Mannitol, Glycerol)

Analgesics: pethidine or morphine (for pain)

OSMOTIC AGENTS

Glycerol 50% syrup (cause nausea, hyperglycemia)

Mannitol 20% IV (cause fluid overload and not used in heart failure)

Dehydrate vitreous body which reduce IOP prior to anterior surgical procedures

Used for short term management of acute rise in IOP

CORTICOSTEROIDS

Mechanism:- Inhibition of arachidonic acid release by inhibiting phospholipase A_2

Topical:-prednisolone, dexamethasone, hydrocortisone

Uses: postoperatively, anterior uveitis, severe allergic conjunctivitis, scleritis, prevention and suppression of corneal graft rejection

Systemic:- prednisolone, cortisone

Uses: posterior uveitis, optic neuritis

Ocular ADRS:-Glaucoma, cataract, skin atrophy, secondary infection, delayed wound healing.

NSAIDS

e.g. ketorolac, diclofenac, flurbiprofen

Mechanism: inhibition of cyclo-oxygenase

Uses: Flurbiprofen preoperatively to prevent miosis following cataract surgery

Diclofenac for postoperative inflammation

Ketorolac for cystoid macular edema occurring after cataract surgery

Side effects: stinging , sterile corneal melt& perforation

TOXICOLOGY

Digitalis causes chromotopsia with overdose

Chloroquine causes retinopathy

Amiodarone causes optic neuropathy & pigmented deposits of the cornea

Phenothizines cause brown pigmentary deposits in the cornea, conjunctiva & eyelid

Sildenafil
Inhibits PDE_5 in the corpus cavernosum to achieve penile erection

It also mildly inhibits PDE_6 which controls the level of cyclic GMP in the retina→ seeing a bluish haze & causing light sensitivity

Steroids → cataract formation, elevated IOP & glaucoma

Ethambutol → optic neuropathy characterized by gradually progressive central scotomas & vision loss